POSTER SESSION 1: LATE EFFECTS/QUALITY OF LIFE/ PSYCHOSOCIAL ISSUES

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Outcomes of Patients with Central Nervous System Complications After Allogeneic Hematopoietic Stem Cell Transplantation

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Background: Allogeneic hematopoietic stem cell transplantation (AHSCT) is a common treatment modality for patients (pts) with hematological disorders. We present a retrospective review of the incidence and impact on outcomes of central nervous system complications (CNSCs) in a cohort of pts with hematological disorders undergoing AHSCT, treated at a single institution.

Methods: 351 pts with hematological disorders who received AHSCT between 2002 and 2011 at an academic medical center were identified. Events that were considered CNSCs included seizures, transient ischemic attack, intracranial hemorrhage, ischemic stroke, subarachnoid hemorrhage, subdural hematoma, meningitis, and posterior reversible encephalopathy syndrome (PRES). Data were obtained from a review of the databases and medical records.

Patient-, disease- and transplant-related characteristics were compared between pts with or without CNSCs. Cumulative incidence of having CNSCs were estimated using death as competing risk. Multivariate Cox proportional hazard regression analysis was used to compare the risk of mortality between pts with or without CNSCs while adjusting for prognostic factors. Prognostic factors considered included: age, sex, disease type, disease stage at transplant, donor-recipient sex-match, cmv status, type of transplant, level of antigen matching, graft type, year of transplant, use of total body irradiation, and prior exposure to cytarabine or cranial irradiation.

Results: Of the 351 pts identified, forty-five pts developed CNSCs (12.8%). No differences in patient-, disease- and transplant-related characterisitcs were noted between those with or without CNSCs. The 100-day cumulative incidence of CNSCs was 8% (95% confidence interval [CI] 8-15%). The most commonly observed CNSCs included: PRES 18 (40%), stroke or TIA 11 (24%), seizures 9 (20%), and infection 4 (9%). In univariate analysis, there was a difference in overall survival (OS) according to CNSCs (log-rank $P = .0002$). The OS at 5 years for pts with CNSCs was 14% (3-32) vs. 44% for pts without CNSCs (P-value 0.0004). In multivariate analysis, the risk of mortality for pts with CNSCs after AHSCT was significantly higher, hazard ratio (HR) 1.56 (95% CI 1.03 − 2.36, $P = .04$) compared to pts without CNSCs. Other prognostic factors identified included: sex, disease type, disease stage at transplant, level of antigen matching. Interestingly, prior history of high dose cytarabine was also associated with higher mortality, HR 2.19 (95% CI 1.51 − 3.18), $P < .0001$.

Conclusion: The incidence of CNSCs after AHSCT is associated with reduced survival. Identifying pts at risk, monitoring, early identification, and treatment for CNSCs post AHSCT is needed to help alter the negative impact on outcomes.

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Incidence and Predictors of Late-Occurring Cirrhosis in Long-Term Survivors of Allogeneic Hematopoietic Cell Transplantation (HCT)

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Background: There is a paucity of knowledge regarding the incidence and predictors of late-occurring cirrhosis that may be due to early post-HCT hepatic complications or late-occurring risk factors such as iron overload, chronic GvHD, or persistent infectious hepatitis in HCT survivors; furthermore, there is limited information regarding the epidemiology of cirrhosis in HCT survivors after the implementation of universal blood product screening for Hepatitis C in 1992.

Methods: Individuals with late-occurring (≥1 year post-HCT) cirrhosis, utilizing World Health Organization criteria, were selected from 1+year survivors of allogeneic HCT performed at a single institution between 1976 and 2007. The National Hospital Discharge Survey was used to compare the HCT cohort with age-, sex-, and HCT year-specific rates of cirrhosis in the general population. Cox proportional hazards regression analysis was used to calculate relative risk (RR) estimates and 95% confidence intervals (CI), adjusted for relevant covariates.

Results: Thirty nine cases of cirrhosis were identified in a cohort of 1,737 HCT survivors, followed for a median of 6.1y (1-33). Median age at HCT: 33.8y (0.6-74.9); median time to cirrhosis: 6.0y (1-25.6); 64% were male; 41% Hispanic; 62% underwent HCT<1992; Hepatitis C infection was present in 56.4%. Cumulative incidence of cirrhosis was 1.6% at 10 yrs and 4.6% at 20 yrs post-HCT. The cohort was at a 15-fold increased risk of cirrhosis (standardized incidence ratio [SIR] 15.0, CI:10.8-20.3) when compared to the general population. The risk was highest for patients who underwent HCT<1992 (SIR=27.9, CI:18.2-40.6); the risk remained elevated among those transplanted ≥1992 (SIR=8.7, CI:5.0-13.8). Absolute excess risk for the entire cohort was 26.2 per 10,000 person-years of follow-up. Multivariable analysis adjusted for age, gender, race/ethnicity, diagnosis, treatment era, HCT conditioning, and GvHD, revealed older age at HCT (>40 yrs [RR=5.9, $P < .01$]) and total body irradiation (TBI [RR=14.4, $P = .01$]) to be independent risk factors for cirrhosis. Five-year survival following diagnosis of cirrhosis was 38.2% (primary cause of death: liver failure in 84.6%)

Conclusions: The incidence of cirrhosis increases with time from HCT. While the risk is higher among those transplanted before 1992, recent HCT recipients remain at increased risk. Older age at HCT and conditioning with TBI significantly increase risk of cirrhosis. These data form the basis for